the model were excluded. Furthermore, the patients with both RA and diabetes were not included in the analysis (n=33). Participants with neither RA nor diabetes were defined as controls.

RA patients, diabetes patients and controls were compared using Cox proportional hazard regression modelling, with age as the time scale. The model was adjusted for sex, smoking status, previous CVD, body mass index (BMI), hypertension, total cholesterol and creatinine. To obtain proportional hazards, an interaction term with age ≤ 75 years vs > 75 years was included for diabetes, smoking and previous CVD. The effects of the groups were compared using overlap of confidence intervals.

Results: Table 1. Participant characteristics

	RA N=387	Diabetes N=2,898	Controls N=63,903
Female sex, n (%)	261 (67)	1,369 (47)	33,781 (53)
Age (yrs), median (IQR)	58 (49-68)	63 (51-73)	46 (34-60)
Never smoker, n (%)	132 (34)	1,263 (44)	29,426 (46)
Former smoker, n (%)	129 (33)	682 (23)	19,010 (30)
Current smoker, n (%)	126 (33)	953 (33)	15,467 (24)
Previous CVD, n (%)	41 (11)	594 (20)	4,094 (6)
BMI (kg/m ²), median (IQR)	26.0 (23.7-29.1)	28.7 (25.9-32.0)	25.7 (23.4-28.4)
Hypertension, n (%)	199 (51)	2,098 (72)	25,333 (40)
Total cholesterol (mmol/l), median (IQR)	6.0 (5.3-6.8)	6.0 (5.1-6.9)	5.7 (4.9-6.5)
Creatinine (μ mol/l), median (IQR)	84 (77, 92)	89 (80, 99)	85 (77, 94)
RA duration (yrs), median (IQR)	6 (3-9)		
Seropositive RA, n (%)	277 (72)		
Diabetes duration (yrs), median (IQR)		5 (2-11)	
Observation time (yrs), median (IQR)	18 (13-19)	17 (8-19)	18 (13-19)

There were 123 (32%) deaths in the RA group, 1280 (44%) deaths in the diabetes groups and 11,641 (18%) deaths in the control group. The hazard ratio (HR) for RA was 1.24 (95% confidence interval: CI 1.02-1.46, p-value 0.013). The HR for diabetes was 1.82 (CI 1.60-2.05, p-value < 0.001) for those aged ≤ 75 years and 1.48 (CI 1.39-1.58, p-value 0.004) for those aged > 75 years. RA patients had a significantly lower HR compared to diabetes patients for age ≤ 75 years, but not for age > 75 years.

Conclusion: Patients with RA or diabetes had significantly higher mortality rates than controls, with larger HR for diabetes than for RA. The HR for RA was significantly lower than for diabetes for patients ≤ 75 years, but not for patients > 75 years. This may be due to survival bias in diabetes patients > 75 years.

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THU0065

VALIDATION OF THE ADJUSTED MULTI-BIOMARKER DISEASE ACTIVITY SCORE FOR PREDICTING RISK OF RADIOGRAPHIC PROGRESSION FOR PATIENTS WITH RHEUMATOID ARTHRITIS

Jeffrey R. Curtis¹, Michael E. Weinblatt², Nancy Shadick², Cecilie Heegaard Brahe³, Mikkel Østergaard³, Merete L. Hetland³, Saedis Saevarsdottir⁴, Megan Horton⁵, Brent Mabey⁵, Darl Flake⁵, Eric H. Sasso⁶, Thomas Huizinga⁷.

¹University of Alabama at Birmingham, Birmingham, United States of America;

²Brigham and Women's Hospital, Boston, United States of America; ³Copenhagen Center for Arthritis Research and DANBIO and University of Copenhagen,

Copenhagen, Denmark; ⁴Karolinska Institutet, Stockholm, Sweden; ⁵Myriad Genetics, Inc., Salt Lake City, United States of America; ⁶Crescendo Bioscience, Inc., South San Francisco, United States of America; ⁷Leiden University Medical Center, Leiden, Netherlands

Background: The multi-biomarker disease activity (MBDA) test has been adjusted to account for the effects of age, sex, and leptin (a surrogate for adiposity) in patients with rheumatoid arthritis (RA).¹ Using data from two cohorts (OPERA study and BRASS registry), this adjusted MBDA

score was shown to be the best individual disease activity measure for predicting radiographic progression, and to provide significant additional information to DAS28-CRP in predicting radiographic progression.

Objectives: To validate the association between the adjusted MBDA score and radiographic progression in two additional cohorts, and to evaluate the MBDA score for predicting risk of radiographic progression in four cohorts combined.

Methods: Four cohorts with requisite data were identified: BRASS registry (N=424), OPERA study (N=164), SWEFOT study (N=235), and Leiden registry (N=163). For the SWEFOT and Leiden cohorts, association of disease activity measures and other factors with radiographic progression (change per year in total Sharp score [TSS]), was evaluated using linear regression. These variables included the adjusted MBDA score, seropositivity (RF and/or ACPA positive), DAS28-CRP, SDAI, CDAI, CRP, baseline total TSS, age, and sex, as available for each cohort. Estimates of risk for radiographic progression (change in TSS > 5) as a function of the adjusted MBDA score were calculated using logistic regression in separate and pooled analyses.

Results: Among the tested measures of disease activity, the leptin-adjusted MBDA score was the most statistically significant univariate predictor of radiographic progression in the SWEFOT (P<0.0001) and Leiden (P<0.0001) cohorts, followed by CRP (p<0.01, in each) (Table). No significant predictive ability was observed for DAS28-CRP, SDAI or CDAI in SWEFOT. DAS28-CRP was a weak predictor in the Leiden cohort (P<0.05), (SDAI, CDAI unavailable). Among non-disease activity variables, baseline TSS and seropositivity were statistically significant predictors, to varying degrees. Neither age nor sex was significant (Table). When DAS28-CRP and the adjusted MBDA score were covariates in the same regression model in the Leiden cohort, DAS28-CRP was not a significant predictor, whereas the adjusted MBDA score remained significant (p=0.000054). When the SWEFOT, Leiden, OPERA and BRASS cohorts were combined (N=986), the adjusted MBDA score remained a significant predictor of radiographic progression, enabling the creation of a risk curve for radiographic progression relative to the continuous adjusted MBDA score.

Conclusion: In two population-based observational cohorts, the adjusted MBDA score was validated and shown to be a more significant predictor of radiographic progression than conventional measures of RA disease activity. Four cohorts were combined to predict risk of radiographic progression using the continuous adjusted MBDA score for the first time.

Table: Univariate linear regression of radiographic progression in the SWEFOT and Leiden cohorts.

Variable	N	SWEFOT		N	Leiden	
		Coefficient (95% CI)	p-value		Coefficient (95% CI)	p-value
MBDA score	235	0.11 (0.057, 0.15)	0.000026	163	0.12 (0.069, 0.16)	0.000002
log(CRP + 1)	235	1.1 (0.35, 1.9)	0.0046	156	1.0 (0.28, 1.8)	0.0076
Seropositivity	181/235	2.7 (0.87, 4.5)	0.004	118/162	1.6 (0.064, 3.2)	0.041
Baseline TSS	235	0.11 (0.012, 0.20)	0.028	163	0.042 (0.024, 0.059)	0.000004
DAS28-CRP	235	0.57 (-0.22, 1.4)	0.16	156	0.67 (0.13, 1.2)	0.016
SDAI	233	0.038 (-0.026, 0.10)	0.24	n/a	n/a	n/a
Male sex	66/235	-0.80 (-2.5, 0.94)	0.37	54/163	-0.36 (-1.9, 1.1)	0.64
CDAI	233	0.016 (-0.058, 0.90)	0.67	n/a	n/a	n/a
Age	235	-0.0094 (-0.067, 0.048)	0.74	163	-0.020 (-0.072, 0.033)	0.46

n/a: not applicable because data needed to compute that variable were not available.

Abstract THU0059 – Table 1

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THU0066

IN EARLY RHEUMATOID ARTHRITIS ANTI-CITRULLINATED PEPTIDE ANTIBODIES ASSOCIATE WITH LOWER NUMBER OF AFFECTED JOINTS, AND IGM RHEUMATOID FACTOR WITH SYSTEMIC INFLAMMATION IN AN ANTI-CITRULLINE DEPENDENT MANNER

Eleftheria Pertsinidou¹, Vivek Anand Manivel¹, Lars Klareskog², Lars Alfredsson^{3,4}, Linda Mathsson^{1,5}, Monika Hansson², Martin Cornillet⁶, Guy Serre⁶, Rikard Holmdahl⁷, Karl Skriver⁸, Per-Johan Jakobsson², Helga Westerlind⁹, Johan Askling⁹, Saedis Saevarsdottir^{2,3}, Johan Rönnelid¹. ¹Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden; ²Karolinska Institute, Rheumatology Unit, Department of Medicine, Solna, Stockholm, Sweden; ³Karolinska Institute, Institute of Environmental Medicine, Stockholm, Sweden; ⁴Stockholm County Council, Center for Occupational and Environmental Medicine, Stockholm, Sweden; ⁵Thermo Fisher Scientific, Uppsala, Sweden; ⁶U1056 Inserm, Toulouse University, Laboratory of Epithelial Differentiation and Rheumatoid Autoimmunity, Toulouse, France; ⁷Karolinska Institute, Department of Medical Inflammation Research, Stockholm, Sweden; ⁸Charité University Hospital, Department of Medicine, Berlin, Germany; ⁹Karolinska Institute, Department of Medicine, Solna, Stockholm, Sweden

Background: Recent studies have shown divergent associations between rheumatoid arthritis (RA)-associated autoantibodies and RA onset phenotype. Whereas some studies report more inflammation in seronegative patients [1, 2], others report that rheumatoid factor (RF) associates with high baseline disease activity [3].

Objectives: To define how individual RA-associated autoantibodies associate with individual disease activity score (DAS28, DAS28CRP) components at the time of RA diagnosis.

Methods: Sixteen individual ACPA reactivities, anti-CCP2, IgA-, IgG- and IgM-RF were analyzed centrally in baseline sera from 1600 RA patients classified according to the 1987 ACR criteria. All antibody cut-offs were determined as the 98th percentile among controls. The results were related to CRP, ESR, number of swollen and tender joints, DAS28, DAS28CRP, global disease activity (visual analogue scale), and health assessment questionnaire obtained at baseline.

Results: Individually, anti-CCP2, IgA RF and IgM RF associated with low counts of swollen and tender joints, with strongest association to anti-CCP2, and with high ESR. The association to low joint counts was stronger to number of individual ACPA reactivities than to anti-CCP2 levels (table). In multiple regression adjusted for age, sex and inclusion year, ACPA number associated strictly with low joint counts whereas IgM RF level associated with increased inflammatory markers, especially ESR (table). Also among IgM RF negative patients, occurrence of ACPA associated with low swollen and tender joint counts. Contrary, among ACPA negative patients, IgM showed no association to elevated ESR. The

Abstract THU0066 – Figure 1

effect of RF on ESR increased with the number of individual ACPA reactivities present, most prominently for IgM RF (figure).

Conclusion: In early RA, ACPA associate with low counts of affected joints and IgM RF associates with elevated ESR in an ACPA-dependent manner. The latter finding relates to in vitro studies showing enhanced inflammatory effect of ACPA immune complexes with addition of RF[4, 5]. Future RA studies relating autoantibodies to disease activity may benefit from evaluating the impact of individual antibodies as well as distinct DAS components separately.

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	IgA RF	IgG RF	IgM RF	ACPA
N (%) antibody positive	692 (43.2)	529 (33.1)	916 (57.2)	1020 (63.8)
Multiple regression:				
CRP P value (β)	0.6914 (0.011)	0.3162 (-0.026)	0.0106 (0.071)	0.6889 (0.011)
ESR P value (β)	0.0215 (0.062)	0.1237 (0.039)	<0.0001 (0.108)	0.0380 (0.057)
SJC P value (β)	0.6175 (0.013)	0.2110 (-0.032)	0.0645 (0.051)	<0.0001 (-0.122)
TJC P value (β)	0.6168 (0.014)	0.4120 (-0.021)	0.8712 (0.005)	0.0007 (-0.094)

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